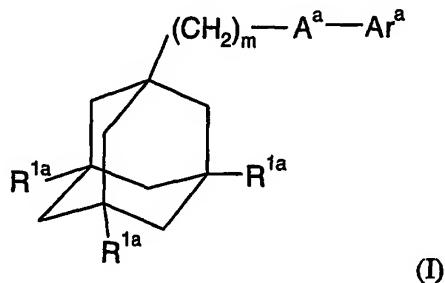


## CLAIMS

1. A pharmaceutical product comprising, in combination, a preparation of a first active ingredient which is a P2X<sub>7</sub> receptor antagonist which P2X<sub>7</sub> receptor antagonist is an adamantyl derivative, and a preparation of a second active ingredient which is a tumour necrosis factor  $\alpha$  (TNF $\alpha$ ) inhibitor, for simultaneous, sequential or separate use in therapy.
- 5
2. A composition according to claim 1 wherein the P2X<sub>7</sub> receptor antagonist is a compound of formula

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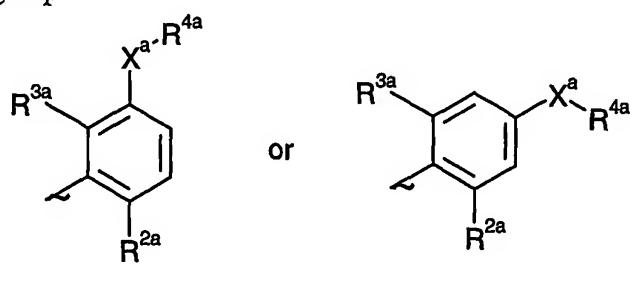


wherein m represents 1, 2 or 3;

each R<sup>1a</sup> independently represents a hydrogen or halogen atom;

15 A<sup>a</sup> represents C(O)NH or NHC(O);

Ar<sup>a</sup> represents a group



X<sup>a</sup> represents a bond, an oxygen atom or a group CO, (CH<sub>2</sub>)<sub>1-6</sub>, CH=, (CH<sub>2</sub>)<sub>1-6</sub>O, O(CH<sub>2</sub>)<sub>1-6</sub>, O(CH<sub>2</sub>)<sub>2-6</sub>O, O(CH<sub>2</sub>)<sub>2-3</sub>O(CH<sub>2</sub>)<sub>1-3</sub>, CR'(OH), (CH<sub>2</sub>)<sub>1-3</sub>O(CH<sub>2</sub>)<sub>1-3</sub>, (CH<sub>2</sub>)<sub>1-3</sub>O(CH<sub>2</sub>)<sub>2-3</sub>O, NR<sup>5a</sup>, (CH<sub>2</sub>)<sub>1-6</sub>NR<sup>5a</sup>, NR<sup>5a</sup>(CH<sub>2</sub>)<sub>1-6</sub>, (CH<sub>2</sub>)<sub>1-3</sub>NR<sup>5a</sup>(CH<sub>2</sub>)<sub>1-3</sub>, O(CH<sub>2</sub>)<sub>2-6</sub>NR<sup>5a</sup>, O(CH<sub>2</sub>)<sub>2-3</sub>NR<sup>5a</sup>(CH<sub>2</sub>)<sub>1-3</sub>, (CH<sub>2</sub>)<sub>1-3</sub>NR<sup>5a</sup>(CH<sub>2</sub>)<sub>2-3</sub>O, NR<sup>5a</sup>(CH<sub>2</sub>)<sub>2-6</sub>O,

$\text{NR}^{5a}(\text{CH}_2)_{2-3}\text{O}(\text{CH}_2)_{1-3}$ ,  $\text{CONR}^{5a}$ ,  $\text{NR}^{5a}\text{CO}$ ,  $\text{S(O)}_n$ ,  $\text{S(O)}_n\text{CH}_2$ ,  $\text{CH}_2\text{S(O)}_n$ ,  $\text{SO}_2\text{NR}^{5a}$  or  $\text{NR}^{5a}\text{SO}_2$ ;

n is 0, 1 or 2;

R' represents a hydrogen atom or a C<sub>1</sub>-C<sub>6</sub> alkyl group;

- 5 one of R<sup>2a</sup> and R<sup>3a</sup> represents a halogen, cyano, nitro, amino, hydroxyl, or a group selected from (i) C<sub>1</sub>-C<sub>6</sub> alkyl optionally substituted by at least one C<sub>3</sub>-C<sub>6</sub> cycloalkyl, (ii) C<sub>3</sub>-C<sub>8</sub> cycloalkyl, (iii) C<sub>1</sub>-C<sub>6</sub> alkyloxy optionally substituted by at least one C<sub>3</sub>-C<sub>6</sub> cycloalkyl, and (iv) C<sub>3</sub>-C<sub>8</sub> cycloalkyloxy, each of these groups being optionally substituted by one or more fluorine atoms, and the other of R<sup>2a</sup> and R<sup>3a</sup> represents a
- 10 hydrogen or halogen atom;

either R<sup>4a</sup> represents a 3- to 9-membered saturated or unsaturated aliphatic heterocyclic ring system containing one or two nitrogen atoms and optionally an oxygen atom, the heterocyclic ring system being optionally substituted by one or more substituents independently selected from fluorine atoms, hydroxyl, carboxyl, cyano, C<sub>1</sub>-C<sub>6</sub> alkyl,

- 15 C<sub>1</sub>-C<sub>6</sub> hydroxyalkyl, -NR<sup>6a</sup>R<sup>7a</sup>, -(CH<sub>2</sub>)<sub>r</sub>NR<sup>6a</sup>R<sup>7a</sup> and -CONR<sup>6a</sup>R<sup>7a</sup>, or R<sup>4a</sup> represents a 3- to 8-membered saturated carbocyclic ring system substituted by one or more substituents independently selected from -NR<sup>6a</sup>R<sup>7a</sup>, -(CH<sub>2</sub>)<sub>r</sub>NR<sup>6a</sup>R<sup>7a</sup> and -CONR<sup>6a</sup>R<sup>7a</sup>, the ring system being optionally further substituted by one or more substituents independently selected from fluorine atoms, hydroxyl and C<sub>1</sub>-C<sub>6</sub> alkyl;

- 20 r is 1, 2, 3, 4, 5 or 6;

R<sup>5a</sup> represents a hydrogen atom or a C<sub>1</sub>-C<sub>6</sub> alkyl or C<sub>3</sub>-C<sub>8</sub> cycloalkyl group;

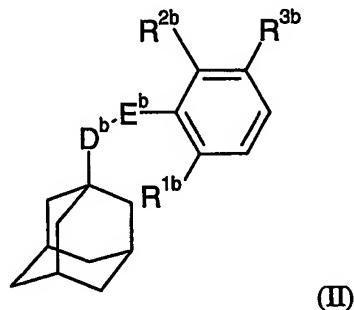
R<sup>6a</sup> and R<sup>7a</sup> each independently represent a hydrogen atom or a C<sub>1</sub>-C<sub>6</sub> alkyl, C<sub>2</sub>-C<sub>6</sub> hydroxyalkyl or C<sub>3</sub>-C<sub>8</sub> cycloalkyl group, or R<sup>6a</sup> and R<sup>7a</sup> together with the nitrogen atom to which they are attached form a 3- to 8-membered saturated heterocyclic ring;

with the provisos that,

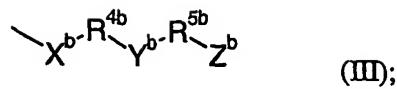
- (a) when A<sup>a</sup> represents C(O)NH and R<sup>4a</sup> represents an unsubstituted 3- to 8-membered saturated aliphatic heterocyclic ring system containing one nitrogen atom, then X<sup>a</sup> is other than a bond, and

- (b) when  $A^a$  represents  $C(O)NH$  and  $X^a$  represents a group  $(CH_2)_{1-6}$  or  $O(CH_2)_{1-6}$ , then  $R^{4a}$  does not represent an unsubstituted imidazolyl, unsubstituted morpholinyl, unsubstituted piperidinyl or unsubstituted pyrrolidinyl group, and
- (c) when  $A^a$  represents  $NHC(O)$  and  $R^{4a}$  represents an unsubstituted 3- to 8-membered saturated aliphatic heterocyclic ring system containing one nitrogen atom, then  $X^a$  is other than a bond, and
- (d) when  $A^a$  represents  $NHC(O)$  and  $X^a$  represents  $O(CH_2)_{1-6}$ ,  $NH(CH_2)_{1-6}$  or  $SCH_2$ , then  $R^{4a}$  does not represent an unsubstituted 1-piperidinyl or unsubstituted 1-pyrrolidinyl group, and
- (e) when  $A^a$  represents  $NHC(O)$  and  $X^a$  represents  $O(CH_2)_{2-3}NH(CH_2)_2$ , then  $R^{4a}$  does not represent an imidazolyl group;
- or a pharmaceutically acceptable salt or solvate thereof.

3. A composition according to claim 1 wherein the  $P2X_7$  receptor antagonist is a compound of formula



- wherein  $D^b$  represents  $CH_2$  or  $CH_2CH_2$ ;
- $E^b$  represents  $C(O)NH$  or  $NHC(O)$ ;
- $R^{1b}$  and  $R^{2b}$  each independently represent a hydrogen or halogen atom, or an amino, nitro,  $C_1-C_6$  alkyl or trifluoromethyl group;
- $R^{3b}$  represents a group of formula



$X^b$  represents an oxygen or sulphur atom or a group NH, SO or  $\text{SO}_2$ ;

$Y^b$  represents an oxygen or sulphur atom or a group  $\text{NR}^{11b}$ , SO or  $\text{SO}_2$ ;

$Z^b$  represents a group -OH, -SH, -CO<sub>2</sub>H, C<sub>1</sub>-C<sub>6</sub> alkoxy, C<sub>1</sub>-C<sub>6</sub> alkylthio,

- 5 C<sub>1</sub>-C<sub>6</sub>-alkylsulphanyl, C<sub>1</sub>-C<sub>6</sub>-alkylsulphonyl, -NR<sup>6b</sup>R<sup>7b</sup>, -C(O)NR<sup>8b</sup>R<sup>9b</sup>, imidazolyl, 1-methylimidazolyl, -N(R<sup>10b</sup>)C(O)-C<sub>1</sub>-C<sub>6</sub> alkyl, C<sub>1</sub>-C<sub>6</sub> alkylcarbonyloxy, C<sub>1</sub>-C<sub>6</sub> alkoxy carbonyloxy, -OC(O)NR<sup>12b</sup>R<sup>13b</sup>, -OCH<sub>2</sub>OC(O)R<sup>14b</sup>, -OCH<sub>2</sub>OC(O)OR<sup>15b</sup> or -OC(O)OCH<sub>2</sub>OR<sup>16b</sup>;

$R^{4b}$  represents a C<sub>2</sub>-C<sub>6</sub> alkyl group;

- 10  $R^{5b}$  represents a C<sub>1</sub>-C<sub>6</sub> alkyl group;

$R^{6b}$ ,  $R^{7b}$ ,  $R^{8b}$ ,  $R^{9b}$ ,  $R^{10b}$ ,  $R^{12b}$  and  $R^{13b}$  each independently represent a hydrogen atom, or a C<sub>1</sub>-C<sub>6</sub> alkyl group optionally substituted by at least one hydroxyl group;

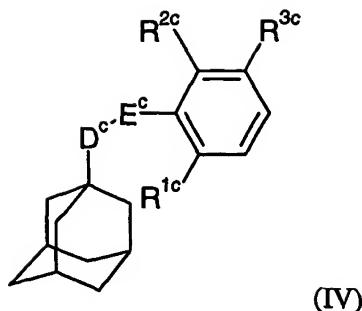
$R^{11b}$  represents a hydrogen atom, or a C<sub>1</sub>-C<sub>6</sub> alkyl group optionally substituted by at least one substituent independently selected from hydroxyl and C<sub>1</sub>-C<sub>6</sub> alkoxy; and

- 15  $R^{14b}$ ,  $R^{15b}$  and  $R^{16b}$  each independently represent a C<sub>1</sub>-C<sub>6</sub> alkyl group;

with the provisos that (i) when  $E^b$  represents NHC(O),  $X^b$  represents O, S or NH and  $Y^b$  represents O, then  $Z^b$  represents -NR<sup>6b</sup>R<sup>7b</sup> where  $R^{6b}$  represents a hydrogen atom and  $R^{7b}$  represents either a hydrogen atom or a C<sub>1</sub>-C<sub>6</sub> alkyl group substituted by at least one hydroxyl group, and (ii) when  $E^b$  represents NHC(O),  $X^b$  represents O, S or NH,  $Y^b$  represents NH and  $R^{5b}$  represents CH<sub>2</sub>CH<sub>2</sub>, then  $Z^b$  is not -OH or imidazolyl;

or a pharmaceutically acceptable salt or solvate thereof.

4. A composition according to claim 1 wherein the P2X<sub>7</sub> receptor antagonist is a compound of formula



wherein  $D^c$  represents  $\text{CH}_2$  or  $\text{CH}_2\text{CH}_2$ ;

$E^c$  represents  $\text{C}(\text{O})\text{NH}$  or  $\text{NHC}(\text{O})$ ;

$R^{1c}$  and  $R^{2c}$  each independently represent hydrogen, halogen, amino, nitro,  $\text{C}_1\text{-}\text{C}_6$  alkyl

5 or trifluoromethyl, but  $R^{1c}$  and  $R^{2c}$  may not both simultaneously represent hydrogen;

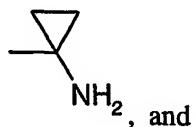
$R^{3c}$  represents a group of formula



$R^{4c}$  represents a  $\text{C}_1\text{-}\text{C}_6$  alkyl group;

10  $X^c$  represents an oxygen or sulphur atom or a group  $\text{NR}^{13c}$ ,  $\text{SO}$  or  $\text{SO}_2$ ;

$R^{5c}$  represents hydrogen, or  $R^{5c}$  represents  $\text{C}_1\text{-}\text{C}_6$  alkyl or  $\text{C}_2\text{-}\text{C}_6$  alkenyl, each of which may be optionally substituted by at least one substituent selected from halogen, hydroxyl, (di)- $\text{C}_1\text{-}\text{C}_6$ -alkylamino,  $-\text{Y}^c\text{-R}^{6c}$ ,



15 a 5- or 6-membered heteroaromatic ring comprising from 1 to 4 heteroatoms independently selected from nitrogen, oxygen and sulphur which heteroaromatic ring may itself be optionally substituted by at least one substituent selected from halogen, hydroxyl and  $\text{C}_1\text{-}\text{C}_6$  alkyl;

$\text{Y}^c$  represents an oxygen or sulphur atom or a group  $\text{NH}$ ,  $\text{SO}$  or  $\text{SO}_2$ ;

20  $\text{R}^{6c}$  represents a group  $-\text{R}^{7c}\text{Z}^c$  where  $\text{R}^{7c}$  represents a  $\text{C}_2\text{-}\text{C}_6$  alkyl group and  $\text{Z}^c$  represents an  $-\text{OH}$ ,  $-\text{CO}_2\text{H}$ ,  $-\text{NR}^{8c}\text{R}^{9c}$ ,  $-\text{C}(\text{O})\text{NR}^{10c}\text{R}^{11c}$  or  $-\text{N}(\text{R}^{12c})\text{C}(\text{O})\text{-C}_1\text{-}\text{C}_6$  alkyl group, and, in the case where  $\text{Y}^c$  represents an oxygen or sulphur atom or a group  $\text{NH}$ ,  $\text{R}^{6c}$  additionally represents hydrogen,  $\text{C}_1\text{-}\text{C}_6$  alkyl,  $\text{C}_1\text{-}\text{C}_6$  alkylcarbonyl,  $\text{C}_1\text{-}\text{C}_6$

alkoxycarbonyl,  $-\text{C}(\text{O})\text{NR}^{14c}\text{R}^{15c}$ ,  $-\text{CH}_2\text{OC}(\text{O})\text{R}^{16c}$ ,  $-\text{CH}_2\text{OC}(\text{O})\text{OR}^{17c}$  or  $-\text{C}(\text{O})\text{OCH}_2\text{OR}^{18c}$ ;

$\text{R}^{8c}$ ,  $\text{R}^{9c}$ ,  $\text{R}^{10c}$ ,  $\text{R}^{11c}$  and  $\text{R}^{12c}$  each independently represent a hydrogen atom or a  $\text{C}_1\text{-C}_6$  alkyl group;

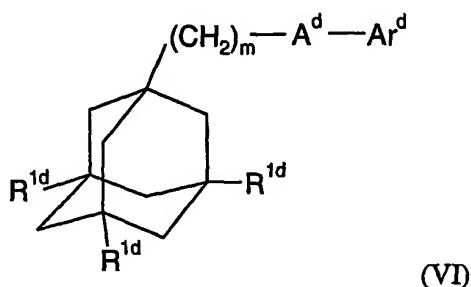
5  $\text{R}^{13c}$  represents hydrogen,  $\text{C}_3\text{-C}_8$  cycloalkyl,  $\text{C}_3\text{-C}_8$  cycloalkylmethyl, or  $\text{R}^{13c}$  represents a  $\text{C}_1\text{-C}_6$  alkyl group optionally substituted by at least one substituent selected from hydroxyl and  $\text{C}_1\text{-C}_6$  alkoxy; and

$\text{R}^{14c}$ ,  $\text{R}^{15c}$ ,  $\text{R}^{16c}$ ,  $\text{R}^{17c}$  and  $\text{R}^{18c}$  each independently represent a  $\text{C}_1\text{-C}_6$  alkyl group; with the proviso that when  $\text{E}^c$  is  $\text{C}(\text{O})\text{NH}$ ,  $\text{X}^c$  is O, NH or  $\text{N}(\text{C}_1\text{-C}_6$  alkyl), then  $\text{R}^{5c}$  is

10 other than a hydrogen atom or an unsubstituted  $\text{C}_1\text{-C}_6$  alkyl group; or a pharmaceutically acceptable salt or solvate thereof.

5. A composition according to claim 1 wherein the  $\text{P}_2\text{X}_7$  receptor antagonist is a compound of formula

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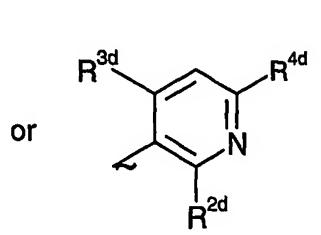
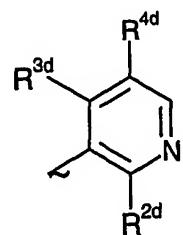
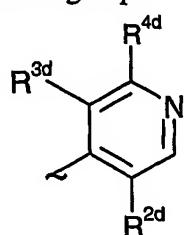


wherein m represents 1, 2 or 3;

each  $\text{R}^{1d}$  independently represents a hydrogen or halogen atom;

20  $\text{A}^d$  represents  $\text{C}(\text{O})\text{NH}$  or  $\text{NHC}(\text{O})$ ;

$\text{Ar}^d$  represents a group



or

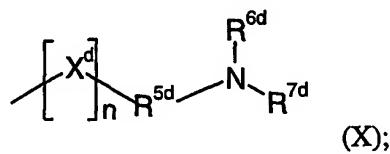
(VII)

(VIII)

(IX)

one of  $R^{2d}$  and  $R^{3d}$  represents halogen, nitro, amino, hydroxyl, or a group selected from (i) C<sub>1</sub>-C<sub>6</sub> alkyl optionally substituted by at least one halogen atom, (ii) C<sub>3</sub>-C<sub>8</sub> cycloalkyl, (iii) C<sub>1</sub>-C<sub>6</sub> alkoxy optionally substituted by at least one halogen atom, and (iv) C<sub>3</sub>-C<sub>8</sub> cycloalkyloxy, and the other of  $R^{2d}$  and  $R^{3d}$  represents a hydrogen or halogen atom;

$R^{4d}$  represents a group



(X);

X<sup>d</sup> represents an oxygen or sulphur atom or a group >N-R<sup>8d</sup>;

10 n is 0 or 1;

R<sup>5d</sup> represents a C<sub>1</sub>-C<sub>5</sub> alkyl group which may be optionally substituted by at least one substituent selected from hydroxyl, halogen and C<sub>1</sub>-C<sub>6</sub> alkoxy;

R<sup>6d</sup> and R<sup>7d</sup> each independently represent a hydrogen atom, C<sub>1</sub>-C<sub>6</sub> alkyl (optionally substituted by at least one substituent selected from hydroxyl, halogen, C<sub>1</sub>-C<sub>6</sub> alkoxy, and (di)-C<sub>1</sub>-C<sub>4</sub> alkylamino (itself optionally substituted by at least one hydroxyl group)), or C<sub>3</sub>-C<sub>8</sub> cycloalkyl (optionally substituted by at least one substituent selected from hydroxyl, halogen and C<sub>1</sub>-C<sub>6</sub> alkoxy); and

R<sup>8d</sup> represents a hydrogen atom or a C<sub>1</sub>-C<sub>5</sub> alkyl group which may be optionally substituted by at least one substituent selected from hydroxyl, halogen and C<sub>1</sub>-C<sub>6</sub> alkoxy;

20 with the provisos that:

(d) when n is 0, then A<sup>d</sup> is NHC(O), and

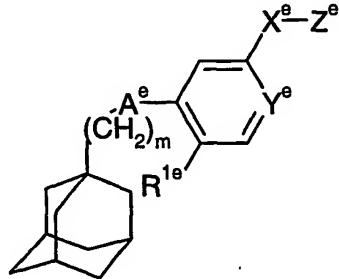
(e) when n is 1, X<sup>d</sup> represents oxygen and A<sup>d</sup> is C(O)NH, then R<sup>6d</sup> and R<sup>7d</sup> do not both simultaneously represent a hydrogen atom or do not both simultaneously represent an unsubstituted C<sub>1</sub>-C<sub>6</sub> alkyl, or when one of R<sup>6d</sup> and R<sup>7d</sup> represents a hydrogen atom, then the other of R<sup>6d</sup> and R<sup>7d</sup> does not represent an unsubstituted C<sub>1</sub>-C<sub>6</sub> alkyl; and

(f) when n is 1, X<sup>d</sup> is oxygen, sulphur or >NH and A<sup>d</sup> is NHC(O), then R<sup>6d</sup> and R<sup>7d</sup> do not both simultaneously represent a hydrogen atom or do not both

simultaneously represent an unsubstituted C<sub>1</sub>-C<sub>6</sub> alkyl, or when one of R<sup>6d</sup> and R<sup>7d</sup> represents a hydrogen atom, then the other of R<sup>6d</sup> and R<sup>7d</sup> does not represent an unsubstituted C<sub>1</sub>-C<sub>6</sub> alkyl or -CH<sub>2</sub>CH<sub>2</sub>OH;  
or a pharmaceutically acceptable salt or solvate thereof.

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6. A composition according to claim 1 wherein the P2X<sub>7</sub> receptor antagonist is a compound of formula



10

(XI)

wherein m represents 1, 2 or 3;

A<sup>e</sup> represents C(O)NH or NHC(O);

Y<sup>e</sup> represents N or CH;

15 X<sup>e</sup> represents a bond, CO, (CH<sub>2</sub>)<sub>1-6</sub>, O(CH<sub>2</sub>)<sub>1-6</sub>, (CH<sub>2</sub>)<sub>1-6</sub>NH(CH<sub>2</sub>)<sub>1-6</sub>, (CH<sub>2</sub>)<sub>1-6</sub>O(CH<sub>2</sub>)<sub>1-6</sub>, NH(CH<sub>2</sub>)<sub>1-6</sub>;

Z<sup>e</sup> represents NR<sup>2e</sup>R<sup>3e</sup>;

20 R<sup>1e</sup> represents halogen, cyano, nitro, amino, hydroxyl, C<sub>1</sub>-C<sub>6</sub> alkyl or C<sub>3</sub>-C<sub>8</sub> cycloalkyl, which alkyl or cycloalkyl group can be optionally substituted by one or more fluorine atoms;

R<sup>2e</sup> and R<sup>3e</sup> each independently represent a hydrogen atom, C<sub>1</sub>-C<sub>6</sub> alkyl or C<sub>3</sub>-C<sub>8</sub> cycloalkyl, which alkyl or cycloalkyl group can be optionally substituted by one or more groups selected from hydroxyl, halogen or C<sub>1</sub>-C<sub>6</sub> alkoxy, or R<sup>2e</sup> and R<sup>3e</sup> together with the nitrogen atom to which they are attached form a 3- to 9-membered saturated mono- or bicyclic heterocyclic ring comprising from 1 to 2 nitrogen

atoms and optionally an oxygen atom, which heterocyclic ring can be optionally substituted by one or more groups selected from hydroxyl, halogen or C<sub>1</sub>-C<sub>6</sub> alkoxy; or a pharmaceutically acceptable salt or solvate thereof.

- 5    7. A composition according to claim 1 wherein the P2X<sub>7</sub> receptor antagonist is:
- 2-Chloro-5-[[2-(2-hydroxy-ethylamino)-ethylamino]-methyl]-N-(tricyclo[3.3.1.1<sup>3,7</sup>]dec-1-ylmethyl)-benzamide,
- 2-Chloro-5-[3-[(3-hydroxypropyl)amino]propyl]-N-(tricyclo[3.3.1.1]dec-1-ylmethyl)-benzamide,
- 10    (R)-2-Chloro-5-[3-[(2-hydroxy-1-methylethyl)amino]propyl]-N-(tricyclo[3.3.1.1<sup>3,7</sup>]dec-1-ylmethyl)-benzamide,
- 2-Chloro-5-[[2-[(2-hydroxyethyl)amino]ethoxy]methyl]-N-(tricyclo[3.3.1.1<sup>3,7</sup>]dec-1-ylmethyl)-benzamide,
- 15    2-Chloro-5-[3-[3-(methylamino)propoxy]propyl]-N-(tricyclo[3.3.1.1<sup>3,7</sup>]dec-1-ylmethyl)benzamide,
- 2-Chloro-5-[3-(3-hydroxy-propylamino)-propoxy]-N-(tricyclo[3.3.1.1<sup>3,7</sup>]dec-1-ylmethyl)-benzamide,
- 2-Chloro-5-[2-(3-hydroxypropylamino)ethylamino]-N-(tricyclo[3.3.1.1<sup>3,7</sup>]dec-1-ylmethyl)-benzamide,
- 20    2-Chloro-5-[2-(3-hydroxypropylsulfonyl)ethoxy]-N-(tricyclo[3.3.1.1<sup>3,7</sup>]dec-1-ylmethyl)-benzamide,
- 2-Chloro-5-[2-[2-[(2-hydroxyethyl)amino]ethoxy]ethoxy]-N-(tricyclo[3.3.1.1<sup>3,7</sup>]dec-1-ylmethyl)-benzamide,
- 25    2-Chloro-5-[[2-[[2-(1-methyl-1H-imidazol-4-yl)ethyl]amino]ethyl]amino]-N-(tricyclo[3.3.1.1<sup>3,7</sup>]dec-1-ylmethyl)-benzamide,
- 2-Chloro-5-piperazin-1-ylmethyl-N-(tricyclo[3.3.1.1]dec-1-ylmethyl)-benzamide,
- 2-Chloro-5-(4-piperidinyloxy)-N-(tricyclo[3.3.1.1<sup>3,7</sup>]dec-1-ylmethyl)-benzamide,
- 2-Chloro-5-(2,5-diazabicyclo[2.2.1]hept-2-ylmethyl)-N-(tricyclo[3.3.1.1]dec-1-ylmethyl)-benzamide,
- 30    2-Chloro-5-(piperidin-4-ylsulfinyl)-N-(tricyclo[3.3.1.1<sup>3,7</sup>]dec-1-ylmethyl)-benzamide,

- 5-Chloro-2-[3-[(3-hydroxypropyl)amino]propyl]-*N*-(tricyclo[3.3.1.1<sup>3,7</sup>]dec-1-ylmethyl)-4-pyridinecarboxamide,
- 2-Chloro-5-[3-[(1*R*)-2-hydroxy-1-methylethyl]amino]propyl]-*N*-(tricyclo[3.3.1.1<sup>3,7</sup>]dec-1-ylmethyl)-3-pyridinecarboxamide,
- 5 5-Chloro-2-[3-(ethylamino)propyl]-*N*-(tricyclo[3.3.1.1<sup>3,7</sup>]dec-1-ylmethyl)-4-pyridinecarboxamide,
- 5-Chloro-2-[3-[(2-hydroxyethyl)amino]propyl]-*N*-(tricyclo[3.3.1.1<sup>3,7</sup>]dec-1-ylmethyl)-4-pyridinecarboxamide,
- 5-Chloro-2-[3-[(2*S*)-2-hydroxypropyl]amino]propyl]-*N*-(tricyclo[3.3.1.1<sup>3,7</sup>]dec-1-ylmethyl)-4-pyridinecarboxamide,
- 10 *N*-[2-Methyl-5-(9-oxa-3,7-diazabicyclo[3.3.1]non-3-ylcarbonyl)phenyl]-tricyclo[3.3.1.1<sup>3,7</sup>]decane-1-acetamide,
- or a pharmaceutically acceptable salt or solvate of any one thereof.
- 15 8. A product according to any one of claims 1 to 7, wherein the second active ingredient is a receptor molecule capable of binding to TNF $\alpha$ .
9. A product according to claim 8 wherein the second active ingredient is Etanercept.
- 20 10. A product according to any one of claims 1 to 7, wherein the second active ingredient is an anti-TNF $\alpha$  antibody.
11. A product according to claim 10, wherein the second active ingredient is selected from Infliximab and Adalimumab (D2E7).
- 25 12. A kit comprising a preparation of a first active ingredient which is a P2X<sub>7</sub> receptor antagonist which P2X<sub>7</sub> receptor antagonist is an adamantyl derivative, a preparation of a second active ingredient which is a tumour necrosis factor  $\alpha$  (TNF $\alpha$ ) inhibitor, and instructions for the simultaneous, sequential or separate administration of the preparations
- 30 to a patient in need thereof.

13. A kit according to claim 12 wherein the P2X<sub>7</sub> receptor antagonist is:

2-Chloro-5-[[2-(2-hydroxy-ethylamino)-ethylamino]-methyl]-N-(tricyclo[3.3.1.1<sup>3,7</sup>]dec-1-ylmethyl)-benzamide,

5 2-Chloro-5-[3-[(3-hydroxypropyl)amino]propyl]-N-(tricyclo[3.3.1.1]dec-1-ylmethyl)-benzamide,

(R)-2-Chloro-5-[3-[(2-hydroxy-1-methylethyl)amino]propyl]-N-(tricyclo[3.3.1.1<sup>3,7</sup>]dec-1-ylmethyl)-benzamide,

2-Chloro-5-[[2-[(2-hydroxyethyl)amino]ethoxy]methyl]-N-(tricyclo[3.3.1.1<sup>3,7</sup>]dec-1-ylmethyl)-benzamide,

10 2-Chloro-5-[3-[3-(methylamino)propoxy]propyl]-N-(tricyclo[3.3.1.1<sup>3,7</sup>]dec-1-ylmethyl)benzamide,

2-Chloro-5-[3-(3-hydroxy-propylamino)-propoxy]-N-(tricyclo[3.3.1.1<sup>3,7</sup>]dec-1-ylmethyl)-benzamide,

15 2-Chloro-5-[2-(3-hydroxypropylamino)ethylamino]-N-(tricyclo[3.3.1.1<sup>3,7</sup>]dec-1-ylmethyl)-benzamide,

2-Chloro-5-[2-(3-hydroxypropylsulfonyl)ethoxy]-N-(tricyclo[3.3.1.1<sup>3,7</sup>]dec-1-ylmethyl)-benzamide,

20 2-Chloro-5-[2-[2-[(2-hydroxyethyl)amino]ethoxy]ethoxy]-N-(tricyclo[3.3.1.1<sup>3,7</sup>]dec-1-ylmethyl)-benzamide,

2-Chloro-5-[[2-[[2-(1-methyl-1*H*-imidazol-4-yl)ethyl]amino]ethyl]amino]-N-(tricyclo[3.3.1.1<sup>3,7</sup>]dec-1-ylmethyl)-benzamide,

2-Chloro-5-piperazin-1-ylmethyl-N-(tricyclo[3.3.1.1]dec-1-ylmethyl)-benzamide,

2-Chloro-5-(4-piperidinyloxy)-N-(tricyclo[3.3.1.1<sup>3,7</sup>]dec-1-ylmethyl)-benzamide,

25 2-Chloro-5-(2,5-diazabicyclo[2.2.1]hept-2-ylmethyl)-N-(tricyclo[3.3.1.1]dec-1-ylmethyl)-benzamide,

2-Chloro-5-(piperidin-4-ylsulfinyl)-N-(tricyclo[3.3.1.1<sup>3,7</sup>]dec-1-ylmethyl)-benzamide,

5-Chloro-2-[3-[(3-hydroxypropyl)amino]propyl]-N-(tricyclo[3.3.1.1<sup>3,7</sup>]dec-1-ylmethyl)-4-pyridinecarboxamide,

2-Chloro-5-[3-[(1*R*)-2-hydroxy-1-methylethyl]amino]propyl]-*N*-  
(tricyclo[3.3.1.1<sup>3,7</sup>]dec-1-ylmethyl)-3-pyridinecarboxamide,  
5-Chloro-2-[3-(ethylamino)propyl]-*N*-(tricyclo[3.3.1.1<sup>3,7</sup>]dec-1-ylmethyl)-4-  
pyridinecarboxamide,  
5-Chloro-2-[3-[(2-hydroxyethyl)amino]propyl]-*N*-(tricyclo[3.3.1.1<sup>3,7</sup>]dec-1-  
ylmethyl)-4-pyridinecarboxamide,  
5-Chloro-2-[3-[(2*S*)-2-hydroxypropyl]amino]propyl]-*N*-(tricyclo[3.3.1.1<sup>3,7</sup>]dec-1-  
ylmethyl)-4-pyridinecarboxamide,  
10 *N*-[2-Methyl-5-(9-oxa-3,7-diazabicyclo[3.3.1]non-3-ylcarbonyl)phenyl]-  
tricyclo[3.3.1.1<sup>3,7</sup>]decane-1-acetamide,  
or a pharmaceutically acceptable salt or solvate of any one thereof.

14. A kit according to any one of claims 12 to 13, wherein the second active ingredient is  
a receptor molecule capable of binding to TNF $\alpha$ .

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15. A kit according to claim 14 wherein the second active ingredient is Etanercept.

16. A kit according to any one of claims 12 to 13, wherein the second active ingredient is  
an anti-TNF $\alpha$  antibody.

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17. A kit according to claim 16, wherein the second active ingredient is selected from  
Infliximab and Adalimumab (D2E7).

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18. Use of a pharmaceutical product or kit according to any one of the preceding claims in  
the manufacture of a medicament for the treatment of an inflammatory disorder.

19. Use according to claim 19, wherein the inflammatory disorder is rheumatoid arthritis.

30

20. A method of treating an inflammatory disorder which comprises simultaneously,  
sequentially or separately administering:

- (a) a (therapeutically effective) dose of a first active ingredient which is a P2X<sub>7</sub> receptor antagonist which P2X<sub>7</sub> receptor antagonist is an adamantyl derivative; and
  - (b) a (therapeutically effective) dose of a second active ingredient which is a tumour necrosis factor  $\alpha$  (TNF $\alpha$ ) inhibitor,
- 5 to a patient in need thereof.
21. A method according to claim 20, wherein the inflammatory disorder is rheumatoid arthritis.